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PANDAS or PARC: A Pediatric Puzzle

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INTRODUCTION

CHILDREN WITH ALLERGIC RHINOCONJUNCTIVITIS (ARC) and pruritus of the eyes, ears, nose, or throat typically respond with facial contortions, such as the "allergic salute" and uninhibited blinking and grimacing that resembles tics. We describe a patient with perennial ARC (PARC) symptoms diagnosed as facial motor tics due to a pediatric autoimmune neuropsychiatric disorder associated with streptococci (PANDAS),(1) and review the literature on this controversial syndrome. (Pediatr Asthma Allergy Immunol 2000;14(2):137–140).

CASE REPORT

An 11-year-old Caucasian boy was evaluated for spasmodic facial movements of 6 months' duration. Abnormalities included forceful blinking, squinting, sniffing, mouth-stretching, grimacing, nose-wrinkling, neck twisting, and upward eye rolling associated with vague itching of the eyes and/or ears and with throat clearing. The symptoms began during the fall when the patient first attempted wearing contact lenses and persisted after he stopped using them. Therapy with oral diphenhydramine was only partly effective. He was initially seen for these complaints by an ophthalmologist and referred to a neurologist. Neuropsychiatric examination showed "multiple facial motor tics" and no other abnormality. The findings did not meet diagnostic criteria for Tourette syndrome (TS),(2) but were interpreted as consistent with PANDAS as summarized in Table 1. Laboratory tests included a complete blood count and thyroid function tests, which were normal; a throat culture, which was negative for Group A beta hemolytic streptococci (GABHS), but positive for non-GABHS. Serologic testing showed antistreptolysin 0 titer of 210 IU/mL (normal <200 IU/mL) and anti-DNAase B titer of >1:2,720 (normal <1:170). The patient was told he had PANDAS and treated with oral phenoxymethylpenicillin V 250 mg daily to prevent streptococcal reinfection; however, there was no change in symptoms during the ensuing 2 months. An allergy/immunology consultation was then requested.

The past medical history was positive for cough ("bronchitis") in spring and fall and mild eczema in infancy. The patient had no prior diagnosis of atopic disease. There was no known hypersensitivity to foods, drugs, contactants, or inhalants. Other family members were healthy, with no history of allergic, infectious, neurologic, or rheumatologic diseases. The patient had no social or scholastic problems. He was not exposed to tobacco smoke or pets at home, although as a young child he had a cat. Review of systems was positive for eyelid crusting after sleep.

Physical examination showed a healthy-appearing, well-developed, and well-nourished boy in no acute distress, wearing glasses. The head, eyes, ears, nose, and throat exam showed allergic shiners, staccato blinking (sometimes followed by a startled expression), and edema of the nasal mucosa. Ophthalmic slit lamp examination revealed mild papillary reaction of the tarsal conjunctivae. The neck, heart, lungs, abdomen, extremities, and neuropsychiatric system were normal. There was pityriasis alba of the left cheek and mild lichenification of the antecubital skin bilaterally.

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TABLE 1. DIAGNOSTIC CRITERIA

Diagnostic criteria for Tourette syndrome(2)
1. Age at onset is between 2 and 15 years.
2. Presence of recurrent, involuntary, repetitive, rapid, purposeless motor movements affecting multiple muscle groups.
3. Multiple vocal tics.
4. Ability to suppress movements voluntarily for minutes to hours.
5. Variations in the intensity of the symptoms over weeks or months.
6. Duration of more than 1 year.

Diagnostic criteria for pediatric autoimmune neuropsychiatric disease associated with streptococci (PANDAS)(1)
1. Presence of OCD and/or tic disorder.
2. Prepubertal onset of symptoms.
3. Episodic course of symptom severity.
4. Association with GABHS infections.
5. Association with neurological abnormalities.

Prick/puncture testing(3) produced immediate hypersensitivity reactions to glycerinated extracts of cat hair and pelt, dust mite (*Dermatophagoides farinae* and *D. pteronyssinus*) and cockroach extracts (Hollister-Stier Laboratories LLC). There was no reactivity to pollens or mold allergens either by skin testing or radioallergosorbent tests (RAST) for allergen-specific IgE.

It was our opinion that the patient's diagnosis was PARC, and that his "tics" were actually the result of "flick blinking" provoked by conjunctival pruritus, compounded by contact lenses.(4) A secondary diagnosis was mild atopic dermatitis. All symptoms improved markedly after initiating treatment with daily cetirizine, montelukast, intranasal mometasone, olopatadine ophthalmic solution, combined with environmental control and subsequent addition of twice-weekly *D. farinae* allergen immunotherapy. After 2 months of this therapy, the patient resumed wearing contact lenses without abnormal blinking. Discontinuation of penicillin prophylaxis was recommended; the other medications and immunotherapy were continued.

DISCUSSION

ARC and tic disorders are prevalent in childhood. Nearly 10% of children have ARC,(5) while tic disorders affect up to 18% of boys and 11% of girls(6,7) (Table 2). Most cases of childhood tic are idiopathic, benign, and self-limited. TS has a lifetime prevalence rate of approximately 1 in 2,000 and is a rare condition in children.(8) There are even fewer cases of PANDAS in the literature, and the prevalence of this disorder is being debated.

In ARC, blepharospasm characteristically presents in association with other signs of atopy, including rhinitis, atopic dermatitis, and/or extrinsic asthma; family history of atopic diseases; ophthalmologic abnormalities including allergic shiners, ocular pruritus, papillary hypertrophy of the tarsal conjunctivae, chemosis, and keratoconus; and laboratory tests showing presence of eosinophils and specific immunoglobulin E (IgE) to seasonal or perennial allergens.(9) IgE to dust mites and animal danders is characteristic of PARC.(10) Our patient had most of these characteristics, and his tic resolved in less than 2 months after therapy for PARC was initiated.

ARC and childhood tic disorders may coexist, and both can produce blepharospasm, further complicating the diagnosis. Finegold reported 4 patients with TS, all of whom had ARC, elevated serum IgE, and sensitivity to dust mite and other aeroallergens.(11) Two of 4 TS patients evaluated by Kim et al. were atopic,(12) and 64% of 72 patients with TS seen consecutively by Ho et al. had elevated total IgE and specific IgE to allergens.(13) However, patients with TS may respond to pruritus or other unpleasant sensations with "sensory tics" such as blepharospasm, eye rolling, squinting, facial grimacing, and nose twitching,(14) which can masquerade as signs of ARC; therefore, distinction may be difficult in an atopic patient with TS. ARC has not been described in association with PANDAS.

There are several reasons for challenging the diagnosis of PANDAS in our patient. As outlined in Table

Table 2. Differential Diagnosis of Tics in Children

I. Primary
  - Transient tic disorder
  - Chronic motor or vocal tic disorder
  - Tourette syndrome
  - Habitual behavior or mannerism
  - Obsessive compulsive disorder
  - Excessive startle

II. Secondary
  - Encephalitis
  - Head trauma
  - Stroke
  - Neuroacanthocytosis
  - Drugs (neuroleptics, carbamazepine, phenytoin, phenobarbital)
  - Toxic substances (carbon monoxide, gasoline)
  - Metabolic disease (Wilson's disease, citrullinemia)
  - Mental retardation +/− chromosomal abnormalities (9p mosaicism, XXX, fragile X, XXY, XYY)
  - Pediatric autoimmune neuropsychiatric disease associated with streptococci (PANDAS)

Modified from Lockman LA. Movement disorders. In: Swaiman KT, Wright FS, eds. The practice of pediatric neurology. St. Louis: Mosby, 1982.

1, PANDAS represents a group of neuropsychiatric disorders characterized by an obsessive compulsive tic with a prepubertal onset, temporal association with GABHS (*Streptococcus pyogenes* infection), episodic clinical course, neurologic abnormalities during an exacerbation, and circulating autoantibodies against basal ganglion neuron antigens. Our patient did not have GABHS infection and an alternative explanation for his symptoms was determined. In addition, although PANDAS hypothetically involves type II hypersensitivity initiated by antibodies to GABHS that cross-react with neurons of the basal ganglia, as is believed to occur in Sydenham's chorea,(15) the association of obsessive compulsive disorder and tic with antistreptococcal and antineuronal antibodies could be coincidental. Indeed, finding a high antistreptococcal antibody titer in a child with tics would not be unexpected given that the majority of school-age children have evidence of a recent or current streptococcal infection.(16) Borderline elevated titers of antistreptolysin O antibody or a positive throat culture occur not only during acute infection, but also in chronically exposed children and pharyngeal carriers.(17) Moreover, 4 months of oral penicillin 250 mg twice daily failed to reduce tic severity in children with PANDAS.(18) The role of the often-cited antineuronal antibodies in obsessive compulsive tic disorders has been questioned as well by investigators unable to detect them in a substantial portion of patients.(19,20) Finally, PANDAS does not fulfill criteria for classification as an autoimmune disease, which requires, in addition to circumstantial evidence, direct evidence based on an acceptable animal model and transfer of disease via pathogenic antibody or T cells.(21)

Therefore, we conclude that our patient's facial motor "tics" were more likely due to PARC than PANDAS. This case emphasizes the need to consider ARC in the differential diagnosis of facial motor tics in children and its potential overlap with TS in atopic children.

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